Appl. No. 09/525,361 Amdt. dated May 8, 2003 Reply to Office Action of December 4, 2002

Amendments to the Specification:

Please re-title the application to read "Methods of diagnosing breast cancer".

Please insert the following heading and paragraph on page 1 following the title and preceding "Field of the Invention".

The application is a continuation-in-part (CIP) of US Application No. 09/439,878, filed November 12, 1999, now abandoned; and a CIP of US Application No. 09/440,370, filed November 12, 1999, now abandoned; and a CIP of US Application No. 09/440,493, filed November 15, 1999, now abandoned; and a CIP of US Application No. 09/440,676, filed November 16, 1999, now abandoned; and a CIP of US Application No. 09/440,677, filed November 16, 1999, now abandoned; and a CIP of US Application No. 09/450,810, filed November 29, 1999, now abandoned; and a CIP of US Application No. 09/453,137, filed December 2, 1999, now abandoned; and a CIP of US Application No. 09/520,478, filed March 8, 2000, now abandoned.

Please amend the paragraph on page 17, lines 17-25 as follows:

In a preferred embodiment, breast cancer sequences are those that are upregulated in breast cancer; that is, the expression of these genes is higher in breast carcinoma as compared to normal breast tissue. "Up-regulation" as used herein means at least about a two-fold change, preferably at least about a three fold change, with at least about five-fold or higher being preferred. All accession numbers herein are for the GenBank sequence database and the sequences of the accession numbers are hereby expressly incorporated by reference. GenBank is known in the art, see, e.g., Benson, DA, et al., Nucleic Acids Research 26:1-7 (1998) and http://www.nebi.nlm.nih.gov/. In addition, these genes were found to be expressed in a limited relative amount or not at all in heart, brain, lung, liver, kidney, prostate, small intestine, testes, fibroblasts and spleen.

Appl. No. 09/525,361 Amdt. dated May 8, 2003 Reply to Office Action of December 4, 2002

Please amend the paragraph at page 21, lines 14-26 as follows:

Another example of a useful algorithm is the BLAST algorithm, described in Altschul et al., J. Mol. Biol. 215, 403-410, (1990) and Karlin et al., PNAS USA 90:5873-5787 (1993). A particularly useful BLAST program is the WU-BLAST-2 program which was obtained from Altschul et al., Methods in Enzymology, 266: 460-480 (1996); http://blast.wustl/edu/blast/READE.html]. WU-BLAST-2 uses several search parameters, most of which are set to the default values. The adjustable parameters are set with the following values: overlap span =1, overlap fraction = 0.125, word threshold (T) = 11. The HSP S and HSP S2 parameters are dynamic values and are established by the program itself depending upon the composition of the particular sequence and composition of the particular database against which the sequence of interest is being searched; however, the values may be adjusted to increase sensitivity. A % amino acid sequence identity value is determined by the number of matching identical residues divided by the total number of residues of the "longer" sequence in the aligned region. The "longer" sequence is the one having the most actual residues in the aligned region (gaps introduced by WU-Blast-2 to maximize the alignment score are ignored).

Please amend the paragraph at page 26, lines 1-6 as follows:

Alternatively, the oligonucleotides may be synthesized on the surface, as is known in the art. For example, photoactivation techniques utilizing photopolymerization compounds and techniques are used. In a preferred embodiment, the nucleic acids can be synthesized in situ, using well known photolithographic techniques, such as those described in WO 95/25116; WO 95/35505; U.S. Patent Nos. 5,700,637 and 5,445,934; and references cited within, all of which are expressly incorporated by reference; these methods of attachment form the basis of the Affimetrix GeneChipTM Affymetrix nucleic acid chip technology, GENECHIPTM, technology.

Please amend the paragraph on page 41, lines 8-25 to read as follows:

"Differential expression," or grammatical equivalents as used herein, refers to both qualitative as well as quantitative differences in the genes' temporal and/or cellular Appl. No. 09/525,361 Amdt. dated May 8, 2003 Reply to Office Action of December 4, 2002

expression patterns within and among the cells. Thus, a differentially expressed gene can qualitatively have its expression altered, including an activation or inactivation, in, for example, normal versus breast cancer tissue. That is, genes may be turned on or turned off in a particular state, relative to another state. As is apparent to the skilled artisan, any comparison of two or more states can be made. Such a qualitatively regulated gene will exhibit an expression pattern within a state or cell type which is detectable by standard techniques in one such state or cell type, but is not detectable in both. Alternatively, the determination is quantitative in that expression is increased or decreased; that is, the expression of the gene is either upregulated. resulting in an increased amount of transcript, or downregulated, resulting in a decreased amount of transcript. The degree to which expression differs need only be large enough to quantify via standard characterization techniques as outlined below, such as by use of Affymetrix GeneChip™ GENECHIP™ expression arrays, Lockhart, Nature Biotechnology, 14:1675-1680 (1996), hereby expressly incorporated by reference. Other techniques include, but are not limited to, quantitative reverse transcriptase PCR, Northern analysis and RNase protection. As outlined above, preferably the change in expression (i.e. upregulation or downregulation) is at least about 50%, more preferably at least about 100%, more preferably at least about 150%, more preferably, at least about 200%, with from 300 to at least 1000% being especially preferred.